

EXHIBIT B
REPLACEMENT PARAGRAPHS

At page 1, lines 6-9 of the specification, the deletions and additions are as shown:

The present application is a nationalization of PCT Application Serial No. PCT/US00/15243, filed June 02, 2000, which claims priority to United States provisional application Serial No. 60/137,470, filed June [4] 04, 1999. The government owns rights in the present invention pursuant to grant number from R37-AG-10488, ROI-DK-14744, and NIH Training Grant T32 AG-AG-DO165, the National Institutes of Health.

At page 1, lines 6-9 of the specification, the final text is as follows:

The present application is a nationalization of PCT Application Serial No. PCT/US00/15243, filed June 02, 2000, which claims priority to United States provisional application Serial No. 60/137,470, filed June 04, 1999. The government owns rights in the present invention pursuant to grant number from R37-AG-10488, ROI-DK-14744, and NIH Training Grant T32 AG-AG-DO165, the National Institutes of Health.

At page 3, lines 14-21 of the specification, the deletions and additions are as shown:

The exemplary ribozymes, designated RZ-1 through RZ-7, cleave the human ER α mRNA at specific nucleotide positions (+377, +889, +894, +956, +1240, +1420, +1680, +1695, +1726 and +2077). They have a characteristic critical region defined by their nucleotide sequences [(SEQ ID NO:1)]. Even minor substitution at this region may result in significant loss of binding activity. The cleavage sites lie within the coding sequence for the DNA-binding domain of the receptor protein. The ribozyme constructs are also effective in inhibiting the progression of quiescent MCF-7 breast cancer cells to the S phase of the cell cycle after their exposure to 17 β -estradiol (10⁻⁹M).

At page 3, lines 14-21 of the specification, the final text is as follows:

The exemplary ribozymes, designated RZ-1 through RZ-7, cleave the human ER α mRNA at specific nucleotide positions (+377, +889, +894, +956, +1240, +1420, +1680, +1695, +1726 and +2077). They have a characteristic critical region defined by their nucleotide sequences. Even minor substitution at this region may result in significant loss of binding

activity. The cleavage sites lie within the coding sequence for the DNA-binding domain of the receptor protein. The ribozyme constructs are also effective in inhibiting the progression of quiescent MCF-7 breast cancer cells to the S phase of the cell cycle after their exposure to 17β -estradiol (10^{-9}M).

At page 4, lines 26-33 of the specification, the deletions and additions are as shown:

The hammerhead ribozymes described here, selectively inhibit estrogen action by [clearing] cleaving the hER α mRNA within its DNA-binding domain. The specifier side arms of both RZ-1 and RZ-2 do not show any significant homology to any known human mRNA species, except three related receptors, hERR-1, hERR-2, and hER β . RZ-2 possesses a slightly greater homology with hER β (90% sequence homology with respect to both side arms) than RZ 1 (one side arm, 90%; the other, 70%). RZ-2 provides a slightly better inhibitory function on the activity of the ERE-TK-Luc plasmid in transfected MCF-7 cells than the RZ1.

At page 4, lines 26-33 of the specification, the final text is as follows:

The hammerhead ribozymes described here, selectively inhibit estrogen action by [clearing] cleaving the hER α mRNA within its DNA-binding domain. The specifier side arms of both RZ-1 and RZ-2 do not show any significant homology to any known human mRNA species, except three related receptors, hERR-1, hERR-2, and hER β . RZ-2 possesses a slightly greater homology with hER β (90% sequence homology with respect to both side arms) than RZ 1 (one side arm, 90%; the other, 70%). RZ-2 provides a slightly better inhibitory function on the activity of the ERE-TK-Luc plasmid in transfected MCF-7 cells than the RZ1.

At page 22, lines 27-31 of the specification, the deletions and additions are as shown:

Positions of other GUC (GUC in RNA and GTC in corresponding cDNA) sequences are 170, 190, 267, 377, 508, 515, 543, 603, 645, 889 (cleavage site within the human mRNA for estrogen receptor for RZ-2), 894 [(cleavage site with the human in mRNA for estrogen receptor for RZ-2)], 956 (cleavage site for [our RZ-1] RZ-1), 1137, 1218, 1240, 1420, 1463, 1468, 1680, 1695, 1726, and 2077. Sites # [894] 889 and 956 were chosen because they met two other requirements, which are:

At page 22, lines 27-31 of the specification, the final text is as follows:

Positions of other GUC (GUC in RNA and GTC in corresponding cDNA) sequences are 170, 190, 267, 377, 508, 515, 543, 603, 645, 889 (cleavage site within the human mRNA for estrogen receptor for Rz-2), 894, 956 (cleavage site for RZ-1), 1137, 1218, 1240, 1420, 1463, 1468, 1680, 1695, 1726, and 2077. Sites # 889 and 956 were chosen because they met two other requirements, which are: